

Appendix  
Amended Claims  
U.S. National Stage of PCT/FR94/00851  
Defective Adenovirus Vectors and Use Thereof in Gene Therapy

1. A defective recombinant adenovirus comprising;
  - the ITR sequences,
  - a sequence permitting the encapsulation,
  - a heterologous DNA sequence,and in which the E1 gene and at least one of the E2, E4 and L1-L5 genes is non-functional.
2. An adenovirus according to claim 1, characterized in that it is of human, animal or mixed origin.
3. (Amended) An adenovirus according to claim 2, characterized in that the adenoviruses of human origin are chosen from those classified in group C.
4. An adenovirus according to claim 2, characterized in that the adenoviruses of animal origin are chosen from adenoviruses of canine, bovine, murine, ovine, porcine, avian or simian origin.
5. (Amended) An adenovirus according to claim 1, characterized in that the E1 and E4 genes are non-functional.
6. (Amended) An adenovirus according to claim 1, characterized in that it is devoid of late genes.
7. An adenovirus according to claim 1, characterized in that it comprises;
  - the ITR sequences
  - a sequence permitting the encapsulation,
  - a heterologous DNA sequence, and
  - a region carrying the gene or part of the gene E2.
8. An adenovirus according to claim 1, characterized in that it comprises:
  - the ITR sequences,
  - a sequence permitting the encapsulation,
  - a heterologous DNA sequence, and
  - a region carrying the gene or part of the gene E4.
9. An adenovirus according to claim 1, characterized in that the E1, E3 and E4 genes are deleted from its genome.
10. An adenovirus according to claim 1, characterized in that the E1, E3, L5 and E4 genes are deleted from its genome.

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11. (Amended) An adenovirus according to claim 1, characterized in that it comprises a functional gene E3 under the control of a heterologous promoter.

12. (Amended) An adenovirus according to claim 1, characterized in that the heterologous DNA sequence comprises one or more genes selected from the group consisting of therapeutic genes and genes encoding antigenic peptides.

13. (Amended) An adenovirus according to claim 12, characterized in that the therapeutic gene is chosen from genes encoding enzymes, blood derivatives, hormones, lymphokines, growth factors, neurotransmitters, precursors of neurotransmitters, synthetic enzymes, trophic factors, apolipoproteins, dystrophin, minidystrophin, tumor suppressor genes, and genes encoding factors involved in coagulation

14. An adenovirus according to claim 12, characterized in that the therapeutic gene is an antisense gene or sequence whose expression in the target cell makes it possible to control the expression of genes or the transcription of cellular mRNAs.

15. An adenovirus according to claim 12, characterized in that the gene encodes an antigenic peptide capable of generating an immune response in man against microorganisms or viruses.

16. An adenovirus according to claim 15, characterized in that the gene encodes an antigenic peptide specific for the Epstein Barr virus, the HIV virus, the hepatitis B virus, the pseudo-rabies virus or alternatively specific for tumours.

17. (Amended) An adenovirus according to claim 12, characterized in that the heterologous DNA sequence also comprises sequences permitting the expression of the one or more heterologous genes in the infected cell.

18. (Amended) An adenovirus according to claim 12, characterized in that the heterologous DNA sequence comprises, upstream of the therapeutic gene, a signal sequence directing the therapeutic product synthesized in the secretory pathways of the target cell.

19. (Amended) A cell line infectible by an adenovirus comprising, integrated into its genome, the functions necessary for the complementation of a defective recombinant adenovirus according to claim 1.

20. (Amended) A cell line according to claim 19, characterized in that it comprises, in its genome the E1 and E2 genes from an adenovirus.

21. (Amended) A cell line according to claim 20, characterized in that it additionally comprises the E4 gene from an adenovirus.

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22. (Amended) A cell line according to claim 19, characterized in that it comprises the E1 and E4 genes from an adenovirus.

23. (Amended) A cell line according to claim 19, characterized in that it additionally comprises the gene for the glucocorticoid receptor.

24. (Amended) A cell line according to claim 19, characterized in that the E2 and E4 genes are placed under the control of an inducible promoter.

25. A cell line according to claim 24, characterized in that the inducible promoter is the LTR promoter of MMTV.

26. (Amended) A cell line according to claim 19, characterized in that the E2 gene encodes the 72 K protein.

27. (Amended) A cell line according to claim 19, characterized in that it is obtained from the line 293.

28. (Amended) A pharmaceutical composition comprising at least one defective recombinant adenovirus according to claim 1.

29. (Amended) A pharmaceutical composition, comprising a recombinant adenovirus according to claim 5.

30. (Amended) A pharmaceutical composition according to claim 28, comprising a vehicle pharmaceutically acceptable for an injectable formulation.

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## SEQUENCE LISTING

## (1) GENERAL INFORMATION:

- (i) APPLICANT: Perricaudet, Michel  
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- (ii) TITLE OF INVENTION: Defective Adenovirus Vectors and Use  
Thereof in Gene Therapy
- (iii) NUMBER OF SEQUENCES: 1
- (iv) CORRESPONDENCE ADDRESS:  
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- (v) COMPUTER READABLE FORM:  
(A) MEDIUM TYPE: Floppy disk  
(B) COMPUTER: IBM PC compatible  
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(D) SOFTWARE: PatentIn Release #1.0, Version #1.30
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- (viii) ATTORNEY/AGENT INFORMATION:  
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- (ix) TELECOMMUNICATION INFORMATION:  
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## (2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 58 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "oligonucleotide"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

AAGCTTATGA AGCGCGCAAG ACCGTCTGAA GATACCTTCA ACCCCGTGTA TCCATATG

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